AF/1647

Atty. Docket No. FAH02 P-300A

CERTIFICATE OF MAILING

I hereby certify that this paper, together with all enclosures identified herein, are being deposited with the United States Postal Service as first class mail, addressed to the Mail Stop Appeal Brief - Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date indicated below.

July 13, 2004
Date

Deborah A. Witvoet
Deborah A. Witvoet

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Art Unit	:	1647
Examiner	:	Regina M. DeBerry
Applicant	:	Gregory M. Fahy, Ph.D.
Appln. No.	:	09/933,309
Filing Date	:	August 20, 2001
Confirmation No.	:	7331
For	:	GROWTH HORMONE THERAPY AND RELATED METHODS AND PHARMACEUTICAL COMPOSITIONS

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

TRANSMITTAL OF APPEAL BRIEF
(PATENT APPLICATION - 37 CFR §1.192)

1. Transmitted herewith, in triplicate, is the APPELLANT'S BRIEF in this application, with respect to the Notice of Appeal filed on May 13, 2004.

2. **STATUS OF APPLICANTS**

This application is on behalf of:

___ other than a small entity.

_X_ a small entity.

A verified statement:

___ is attached.

_X_ was already filed.

3. **FEE FOR FILING APPEAL BRIEF**

Pursuant to 37 CFR §1.17(c), the fee for filing the Appeal Brief is:

X	small entity	$165.00
___	other than a small entity	$330.00
	Appeal Brief fee due:	$165.00

4. **EXTENSION OF TERM**

The proceedings herein are for a patent application and the provisions of 37 CFR §1.136 apply.

If an additional extension of time is required, please consider this a petition therefor.

(b) X Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

5. **TOTAL FEE DUE**

The total fee due is:

Appeal Brief fee:	$165.00
Extension fee (if any)	$ 0.00
TOTAL FEE DUE:	$165.00

6. **FEE PAYMENT**

X Attached is a check in the sum of $165.00

___ Charge Account No. 16 2463 the sum of $_____.

A duplicate of this transmittal is attached.

7. FEE DEFICIENCY

_X_ If any additional extension and/or fee is required, this is a request therefor and to charge Account No. 16 2463.

and/or

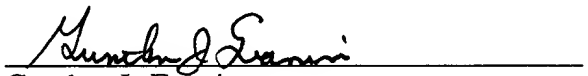
_X_ If any additional fee for claims is required, charge Account No. 16 2463.

Respectfully submitted,

GREGORY M. FAHY, PH.D.

By: Price, Heneveld, Cooper, DeWitt & Litton, LLP

July 13, 2004
Date



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APPELLANT'S BRIEF (37 CFR §1.192)

This brief is in furtherance of the Notice of Appeal filed May 13, 2004.

The fees required under §1.17(f), and any required petition for extension of time for filing this brief and fees therefor, are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This brief is transmitted in triplicate. (37 CFR §1.192(a)).

This brief contains these items under the following headings, and in the order set forth below (37 CFR §1.192(c)):

I. Real Party in Interest
II. Related Appeals and Interferences
III. Status of Claims
IV. Status of Amendments
V. Summary of Invention
VI. Issues
VII. Grouping of Claims
VIII. Arguments
IX. Conclusion

Appendix of Claims Involved in the Appeal

The final page of this brief bears the attorney's signature.

I. Real Party in Interest

The real party in interest in this application is Gregory M. Fahy, Box 478, Norco, California, 92860.

II. Related Appeals and Interferences

There are not any related appeals or interferences which will directly affect, or be directly affected by, or have a bearing on, the Board's Decision in this Appeal.

III. Status of Claims

This is an Appeal from the rejection of all pending claims 16-22 and 32-34. The remaining claims have been cancelled.

IV. Status of Amendments

Appellant has not filed an amendment after the Final Rejection. All previous amendments were entered.

V. Summary of the Invention

The invention relates to a process for preparing a patient for an organ transplant or tissue graft. In particular, the method reduces the risk of organ or tissue rejection. The method also has the advantage of reducing or eliminating the need for immunosuppression. The steps of the claimed method include regenerating a patient's thymus (such as by utilizing human growth hormone (HGH) therapy, preferably in combination with administration of dehydroepiandrosterone or its equivalent); and thereafter injecting into the regenerated thymus donor-specific cells or antigens that are the immunological equivalent of the tissue that is to be transplanted or grafted. This treatment has the effect of making the patient's immune system

tolerant to the donor tissue. Once this is accomplished, the organ transplant or tissue graft is performed using conventional surgical techniques.

VI. Issues

The issues under consideration in this Appeal are as follows:

A. Whether claim 16 meets the definiteness requirement under 35 U.S.C. §112, second paragraph.

B. Whether claims 16-22 and 32-34 are enabled by the specification in view of the prior art under 35 U.S.C. §112, first paragraph.

VII. Grouping of Claims

For purposes of this Appeal only, claim 16 stands or falls by itself with respect to the indefiniteness rejection under 35 U.S.C. §112, second paragraph; and claims 16-22 and 32-34 stand or fall together with respect to the lack of enablement rejection under 35 U.S.C. §112, first paragraph.

VIII. Arguments

A. Claim Rejections Under 35 U.S.C. §112, Second Paragraph

Claim 16 remains improperly rejected under 35 U.S.C. §112, second paragraph, on grounds that it is indefinite for failing to particularly point out and distinctly claim the subject matter which Appellant regards as the invention. The Examiner has stated that the basis for the rejection was set forth in pages 3 and 4 of the previous Office Action. In that Office Action, the Examiner stated that "Claim 16 is drawn to a method for transplanting organs and grafting tissue into a patient comprising: restoring immune system function by regenerating the patient's involuted thymus; injecting the immunological equivalent of the tissue or organ to be transplanted into the patient, into the regenerated thymus (or, in the case of bone marrow cell, peripherally); and then transplanting said organ or grafting said tissue." In the above quotation, the Examiner correctly recited and/or characterized the subject matter of claim 16.

After correctly reciting claim 16, in an attempt to support the rejection, the Examiner stated the following:

> The claim is indefinite because it is drawn to regenerating the patient's involuted thymus but the steps comprise injecting the immunological equivalent into the regenerated thymus (which means the thymus is already regenerated). Thus, the steps of regenerating the involuted thymus have not been taught. The claim does not set forth any steps involved in the method/process (regenerating an involuted thymus). It is unclear what methods/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The statement that the claim is drawn to regenerating the patient's involuted thymus is incorrect. This incorrect characterization of the claim may have led to an erroneous conclusion that claim 16 is indefinite. As the Examiner had previously stated, "claim 16 is drawn to a method for transplanting organs and grafting tissue into a patient," not to a method for "regenerating the patient's involuted thymus." The Examiner may have meant to say that the claim is indefinite because it is drawn to a method for transplanting organs and grafting tissue, but the steps comprise injecting the immunological equivalent into the regenerated thymus (which means the thymus is already regenerated). However, this is not a proper argument. There is nothing indefinite about injecting the immunological equivalent of the tissue or organ to be transplanted into a thymus that has been regenerated. The fact that the thymus has already been regenerated before the immunological equivalent material is injected into the thymus is expressly required by the claim. The first step is "restoring immune system function by regenerating the patient's involuted thymus."

It is unclear what the Examiner is attempting to say by stating that the "steps of regenerating the involuted thymus have not been taught." Whether the steps of regenerating the involuted thymus have or have not been taught is not relevant to a rejection under 35 U.S.C. §112, second paragraph. Accordingly, we will only address definiteness issues under 35 U.S.C. §112, second paragraph, and assume that the Examiner's statement that "the steps of regenerating the involuted thymus have not been taught," were inadvertent and irrelevant.

The Examiner's statement that the claim does not set forth any steps involved in the process for regenerating an involuted thymus is confusing and apparently irrelevant. Appellant has not claimed a process for regenerating an involuted thymus. As stated by the Examiner, claim 16 is directed to a method for transplanting organs and grafting tissue into a patient, not a process for regenerating an involuted thymus. Appellant submits that the statement that the "claim does not set forth any steps involved in the method/process (regenerating an involuted thymus)," was inadvertent and is irrelevant.

The Examiner has stated that "It is unclear what method/process Applicant is intending to encompass." This is evident from the fact that the Examiner has repeatedly and incorrectly stated that Appellant is claiming a method for regenerating an involuted thymus, while inconsistently acknowledging that claim 16 is drawn to a method for transplanting organs and grafting tissue. The Examiner's failure to focus on the claims as written is not a proper basis for rejection under the United States Patent Laws.

Finally, the Examiner has stated that a claim is indefinite "where it merely recites a use without any active, positive steps delimiting how this use is actually practiced." Appellant's claims recite active, positive steps delimiting how the claimed method for transplanting organs and grafting tissue into a patient is actually practiced. These steps include: "restoring immune system function by regenerating the patient's involuted thymus; injecting the immunological equivalent of the tissue or organ to be transplanted into the patient, into the regenerated thymus (or, in the case of bone marrow cells, peripherally); and then transplanting said organ or grafting said tissue." Restoring, injecting and transplanting are all active, positive steps that delimit how the claimed method of transplanting organ and grafting tissue is actually practiced. Accordingly, the Examiner's statement is incorrect.

The Examiner has further stated as follows:

> Claim 16 is indefinite because the term 'immunological equivalent' is a relative term which renders the claim indefinite. The term 'immunological equivalent' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The primary purpose of the definiteness requirement is to ensure that the scope of the claims is clear so that the public is informed of the boundaries of what constitutes infringement of the patent. The language of the claims is sufficiently definite to ensure that the scope of the claims is clear enough so that the public is informed of the boundaries of what constitutes infringement of the patent. Specifically, the expression "immunological equivalent" is frequently used in the literature, and means that the immunologically equivalent material induces an immunological effect equivalent to a specific material, e.g., the tissue or organ to be transplanted into a patient. Those having ordinary skill in the art would not regard the expression "immunological equivalent" as a relative term. A material either is or is not the immunological equivalent of the organs and/or tissue grafted into the patient. In other words, the material either does or does not induce an immunological effect equivalent to the tissue or organ to be transplanted. Thus, the term "immunological equivalent" is not a term of degree, and therefore is not a relative term. Regardless, the fact that claim language includes terms of degree, and may not be precise, does not automatically render the claim indefinite. *Seattle Box Co. v. Industrial Crating and Packing, Inc.*, 731 F.2d 818, 221 USPQ 568 (Fed. Cir. 1984). Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed in light of the specification. The specification states that donor-specific cells or antigens that are the immunological equivalent of the tissue itself are materials that stimulate "deletion or anergy of the cells otherwise responsible for later rejecting the transplanted tissue or organ," and include "endogenously-derived sample in the case of those with autoimmune diseases . . ." Those having ordinary skill in the art are adequately informed by the specification, and would have been fully aware of what constitutes immunological equivalent materials within the context of the claimed invention. Specifically, the person of ordinary skill would be capable of determining whether a particular material stimulates deletion or anergy of the cells otherwise responsible for later rejecting the transplanted tissue or organ, and therefore would be capable of determining with reasonable certainty the boundaries of what constitutes infringement of the claim. Thus, the requirements of 35 U.S.C. §112, second paragraph, have been satisfied.

The Examiner has stated the following:

> The Examiner never used the word 'enablement' in the 35 U.S.C. 112, second paragraph rejection, so it is unclear why Applicants think the distinction between 112, first paragraph and 112, second paragraph have been confused. The Examiner used a form paragraph (paragraph 7.34.01) to make the instant rejection. Please see MPEP 706.03(d).

As pointed out above, in presenting arguments in support of the rejection of claim 16 under 35 U.S.C. §112, second paragraph, the Examiner stated that "the steps of regenerating the involuted thymus have not been taught." Thus, while the Examiner never used the word "enablement" in the 35 U.S.C. §112, second paragraph rejection, the statement that "the steps of regenerating the involuted thymus have not been taught" implies lack of enablement. While the Examiner stated that a form paragraph was used, it should be noted that the form paragraph from the MPEP does not include the words "the steps of regenerating the involuted thymus have not been taught," or any similar words. The above quoted statement is not relevant to definiteness under 35 U.S.C. §112, second paragraph, and is only relevant to patentability of claims based on the enablement requirement of 35 U.S.C. §112, first paragraph. Nevertheless, the Examiner is now insisting that enablement is not an issue. Thus, Appellant will assume that the enablement issues implied in the original rejection were inadvertent, irrelevant and implicitly withdrawn by the Examiner with respect to the indefiniteness rejection under 35 U.S.C. §112, second paragraph.

The Examiner has now acknowledged that Appellant is claiming "a method for transplanting organs and grafting tissue into a patient," with one of the steps comprising "restoring immune system function by regenerating the patient's involuted thymus." As noted above, the Examiner was previously confused as to whether Appellant was claiming a method for transplanting organs and grafting tissue, or a method for restoring immune function in a patient's involuted thymus.

The Examiner has apparently abandoned the previous arguments in support of a rejection under 35 U.S.C. §112, second paragraph, but has maintained the rejection on

different grounds. Specifically, the Examiner has stated as follows:

> The MPEP states, a claim which fails to interrelate essential elements of the invention as defined by Applicants in the specification may be rejected under 35 U.S.C. 112, second paragraph, for failure to point out and distinctly claim the invention (MPEP 2172.01). Regenerating the patient's involuted thymus is part of the steps of the method claim. Contrary to Applicants' assertion, the steps *do* [emphasis in original statement] comprise injecting the immunological equivalent into a regenerated thymus (lines 4-5 of claim 16). The steps recite that immune system function is first restored by regenerating the thymus, and then the immunological equivalent is injected into the regenerated thymus. Furthermore, the Examiner recited references provide by Applicants in the IDS to demonstrate lack of enablement (page 5, last Office Action). The recital of references in the 112, first paragraph rejection has no bearing on the 112, second paragraph rejection of claim 16.

The above quoted basis for rejecting claim 16 under 35 U.S.C. §112, second paragraph, is very confusing. Appellant agrees that the steps of the method for transplanting organs and grafting tissue include "regenerating the thymus, and then the immunological equivalent is injected into the regenerated thymus." This is merely paraphrasing the claim, not an explanation as to what essential elements of the invention are omitted from the claim or have not been properly interrelated. The remainder of the Examiner's statement is apparently irrelevant. Specifically, the statements that the Examiner has cited references that "demonstrate lack of enablement," and that these "recitals" have "no bearing on the 112, second paragraph rejection of claim 16," represent an introduction of enablement issues and a subsequent disclaimer of enablement issues. Regardless, there is not any explanation as to how a rejection based on failure to interrelate essential elements of the invention is justified. It is respectfully submitted that the essential steps have been recited and properly interrelated. Accordingly, the rejection is improper and should be reversed.

It should be noted that contrary to the Examiner's statement, Appellant never asserted that the steps *do not* comprise injecting the immunological equivalent of the organs or tissue

to be transplanted into a patient's regenerated thymus. Appellant's statement was that "the steps do not merely comprise 'injecting the immunological equivalent into the regenerated thymus,' but instead, first, require a step of 'restoring immune system function by regenerating the patient's involuted thymus."

The Examiner has incorrectly stated that "Applicants maintain that it is intentional that the claim does not set forth any steps involved in the method/process (regenerating an involuted thymus)." Appellants are claiming "A method for transplanting organs and grafting tissue into a patient," not a method for "regenerating an involuted thymus." This fundamental misunderstanding may be the basis for much of the Examiner's confusion. The Examiner claims to understand that a method of transplanting organs and grafting tissues is not a method of restoring immune function by regenerating a patient's involuted thymus, but nevertheless has stated as follows:

> The Examiner understands that 'a method for transplanting organs and grafting tissues' is in the preamble, *however*, [emphasis in original rejection] the steps of the claimed method comprise *both* [emphasis in original rejection] regenerating a thymus and transplanting organs and grafting tissue. Applicants assert that it is not necessary to limit the method of transplanting organs and grafting tissue into a patient by using any particular step of restoring immune system function by regenerating the patient's involuted thymus and that particular techniques for restoring immune function are the subject matter of dependent claims 20-23. This is incorrect because the thymus must be regenerated before the immunological equivalent can be injected. The claim is indefinite because it fails to set forth the steps involving regenerating the thymus. The omitted steps of regenerating the thymus are essential to the method of claim 16.

It appears that the Examiner is attempting to argue that claim 16 is indefinite because it fails to set forth essential limitations relating to the step of regenerating the thymus. The Examiner's reasoning that additional limitations are required because "the thymus must be regenerated before the immunological equivalent can be injected" is incorrect. The claim clearly requires that the thymus must be regenerated before the immunological equivalent material is injected. This is also evident from the requirement that the immunological

equivalent of the tissue or organ to be transplanted is injected "into the regenerated thymus." The claim is not indefinite merely because it does not include further limitations that more specifically restrict the technique used for regenerating the thymus. While those having ordinary skill in the art would be provided with an opportunity to more easily avoid infringement if the claims were more narrowly directed to regenerating the patient's thymus by administering HGH, HGH analogs, HGH precursors, HGH metabolites, HGH releasers, HGH mimics, or mixtures thereof, as required in claim 20, the standard by which definiteness is determined is not based on the ease by which infringement can be avoided. An important, pioneering invention of the type claimed cannot be rejected as being indefinite merely because it is not written narrowly enough to allow competitors to easily avoid infringement. Those having ordinary skill in the art can determine whether a patient's involuted thymus is regenerated prior to injection of the immunological equivalent tissue or organ into the patient's regenerated thymus. Therefore, the public can determine the boundaries of what constitutes infringement. Accordingly, the claims fulfill the primary purpose of the definiteness requirement.

The requirement that steps essential to practicing the invention must not be omitted from the claims, is limited to the situation in which the claim "omits matter disclosed to be essential to the invention as described in the specification or in other statements of record." *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Appellant regards his invention to be a "method for transplanting organs and grafting tissue into a patient," not a method of restoring immune function by regenerating a patient's involuted thymus. There is not any statement in the specification or on the record that would indicate that the Appellant regards a particular technique of regenerating the thymus to be essential to the claimed invention. To the contrary, at page 17, lines 1-4, of the specification, the Appellant has stated that "In broader aspects of thymic regeneration to facilitate thymic injection and subsequent organ and tissue transplantation, alternative methods for regenerating the thymus can be utilized." Disclosed examples include "the use of zinc alone, Vitamin E alone, or coenzyme Q_{10} alone . . ." Thus, rather than teaching that HGH or its analogs, precursors, metabolites, releasers, and mimics

are essential to the claimed invention, the Appellant has expressly stated that there are other techniques that may be utilized in the broader aspects of the invention. Clearly, claim 16 does not omit essential matter.

Finally, in the protracted and unfocused rejection of claim 16 under 35 U.S.C. §112, first paragraph, the Examiner has argued that the meaning of the expression "immunological equivalent" is not defined in the specification. The Examiner's statement reads as follows:

> The specification uses 'immunological equivalent' in a sentence but fails to specifically teach the definition of 'immunological equivalent.' The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

The mere fact that the specification does not use the word "definition" in defining the meaning of the expression "immunological equivalent" does not mean that the specification fails to define the term. The passage in which the term "immunological equivalent" is defined (page 15, line 18 through page 16, line 9) reads in its entirety as follows:

> After thymic regeneration, the thymus should be imaged (preferably by magnetic resonance imaging, though other methods are also acceptable) to verify regeneration and thymic location. Surgery should then take place on the same day as or on the day after HGH and DHEA are administered according to the protocol specified above. At this time, a surgeon skilled at thymic biopsy retrieval injects into the thymus an appropriate sample of the tissue or organ to be transplanted later, or injects any other donor-specific cells or antigens (for example, bone marrow cells) that are the immunological equivalent of the tissue itself in stimulating deletion or anergy of the cells otherwise responsible for later rejecting the transplanted tissue or organ. This tissue may be an endogenously-derived sample in the case of those with autoimmune diseases, e.g., myelin from the cauda equina to reverse multiple sclerosis; a joint biopsy to reverse autoimmune arthritis; or endogenous islets to reverse incipient diabetes in the case of diabetes that has not progressed to the point of major islet die-off. The amount of injected tissue is equivalent to 1/10th to twice the amount specified by the Naji prior art for animals without thymic atrophy (based on the ratio of thymic volume to volume of the injected tissue and/or on the ratio of the volume of injected tissue to body weight). A

> variation on direct intrathymic injection is peripheral injection of cells that spontaneously migrate to the regenerated thymus (e.g., bone marrow cells) and thus induce tolerance.

When properly read in the context of the specification, it is clear to one having ordinary skill in the art that Appellant is defining the expression "immunological equivalent" as a material that is the "immunological equivalent of the tissue itself in stimulating deletion or anergy of the cells otherwise responsible for later rejecting the transplanted tissue or organ." In addition to expressly defining the meaning of the term "immunological equivalent," the Appellant has provided several specific examples to further illustrate the meaning of the term and define the invention with reasonable certainty such that the public is fairly put on notice as to the metes and bounds of the invention.

According to MPEP §2173.02, it is incumbent upon the Examiner to allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. The MPEP further states as follows:

> Some latitude in the manner of expression and the aptness of term should be permitted even though the claim language is not as precise as the Examiner might desire. Examiners are encouraged to suggest claim language to Appellants to improve the clarity or precision of the language used, but should not reject claims or insist on their own preferences if other modes of expression selected by Appellants satisfy the statutory requirements. The essential inquiry pertaining to the definiteness requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) the content of the particular application disclosure; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

In view of the specification, it is respectfully submitted that one possessing the ordinary level of skill in the pertinent art at the time the invention was made would understand what was meant by the expression "immunological equivalent." More specifically, applying Appellant's

definition, those having ordinary skill in the art would be able to determine with a reasonable degree of certainty whether they are practicing the claimed method by injecting into the thymus a material that stimulates deletion or anergy of cells otherwise responsible for rejection of subsequently transplanted tissue or organ, prior to transplanting a tissue or organ.

The Examiner's statement that the scientific reasoning and evidence as a whole indicates that the rejection should be maintained is an unsupported conclusion. The Examiner has not provided any reasoning or evidence that would indicate that the rejection should be maintained. To the contrary, the rejection does not properly or completely consider the evidence of record, including the disclosure in the specification, and is not based on a proper interpretation of the claim. Thus, the rejection of claim 16 under 35 U.S.C. §112, second paragraph, is inappropriate and must be reversed.

B. Claim Rejections Under 35 U.S.C. §112, First Paragraph

All pending claims (16-22 and 32-34) remain rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner has stated that the basis for the rejection is set forth at pages 4-7 of the previous Office Action (dated April 4, 2003).

The Examiner has stated that "The instant specification fails to demonstrate that a patient can have an involuted thymus regenerated, then undergo an intrathymic injection and organ transplant or tissue graft." This is incorrect. The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent application coupled with information known in the art without undue experimentation. A patent need not teach, and preferably omits, that which is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ.2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonol Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied,* 480 US 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

The Examiner has admitted that the prior art teaches that an involuted thymus can be regenerated. Specifically, the Examiner has stated as follows:

> Greenstein et al. (J. Endocr. 1987, IDS submitted by Applicant) teach orchidectomy is associated with an increased immune response to antigen challenge. Greenstein demonstrates that the thymus, which had virtually disappeared in old rats, was greatly restored after orchidectomy. Greenstein also demonstrates that regeneration of an age-involuted thymus can be accomplished in rats using an analogue of luteinizing hormone-releasing hormone (LHRH). The LHRH analog, however, also reduced testosterone concentrations to a level measured in orchidectomized rats. McCormick et al. (Aging: Immunology and infectious Disease, 1991, IDS submitted by Applicant) teach that regeneration of an age-involuted thymus can be accomplished in rats using growth hormone (GH). However, there was no significant improvement of cellular immune function and most importantly, there was a high incidence of hepatic tumors noted in the growth hormone treated mice. Goff et al. (Clin. Exp. Immunol., 1987, IDS submitted by Applicant, Paper No. 3) discloses the dubious nature of discerning a regenerated thymus. Goff states, 'a change (or lack of change) in thymic morphology does not prove increased or decreased thymic function: immunological or endocrine function must also be assessed' (page 585, 3rd paragraph).

Thus, the Examiner has admitted that both the Greenstein et al. and McCormick et al. references teach that regeneration of an involuted thymus is well known to those possessing ordinary skill in the art. Further, the specification expressly teaches techniques for regenerating an involuted thymus, such as "administering by subcutaneous injection or other efficacious route every day or every other day or three times a week (e.g., Monday, Wednesday and Friday) at an HGH equivalent dose of 0.01 to 0.05 mg/kg of body weight, the dose being adjusted to avoid peak levels of growth hormone or somatomedin C greater than those found in individuals that are 10-30 years of age" (page 6, lines 4-9 of the specification). Thus, the specification, the evidence of record, and the Examiner's own statements show that regeneration of an involuted thymus is well known to those having ordinary skill in the art and is adequately described in the specification to provide enablement to those having ordinary skill in the art. In view of the fact that the Appellant provided a specific treatment regimen for regenerating an involuted thymus, and in view of the fact that the prior art discloses similar

techniques for regenerating a thymus, it is respectfully submitted that the disclosure coupled with information known in the art would provide the necessary enablement for regenerating a human thymus.

A surgeon skilled at thymic biopsy retrieval (one of ordinary skill in the art) would know how to achieve the intrathymic injection without undue experimentation, and a skilled transplant surgeon would know how to transplant an organ or graft a tissue without undue experimentation. Accordingly, each of the individual steps of the claimed method may be achieved by those having ordinary skill in the art without undue experimentation. The Examiner has admitted the same. At page 9 of the Final Rejection, the Examiner stated as follows:

> Regenerating a thymus in laboratory animals is known in the art. Intrathymic injection in laboratory animals is known in the art. The combination of intrathymic injection and transplantation of organs and grafting of tissue in laboratory animals is known in the art. Transplantation of organs and grafting tissue in humans and laboratory animals is known in the art.

This is a clear admission by the Examiner that the individual steps are known and are enabled. Normally, if all of the steps of a claimed process are enabled, the claimed process is enabled. However, the Examiner has taken the position that despite the fact that each of the individual steps are enabled, somehow the claimed method is not enabled.

The Examiner has stated that the specification is not enabling because "Applicants have not demonstrated that this combined method would be successful or better than the methods known in the art for organ transplant/tissue grafts." There is not any legal requirement that the Appellant prove with absolute certainty that the claimed method would be successful in all cases, or that the Appellant demonstrate that the claimed method is better than known methods. The law is clear on these points. First, an Appellant need not have actually reduced the invention to practice. *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987). The mere fact that something has not previously been done is not, in itself, a sufficient basis for rejection. *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325 (CCPA 1956).

When considering the factors relating to a determination of non-enablement, if all the other factors point toward enablement, then the absence of working examples will not by itself render the invention non-enabled. Lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement. Here, the Examiner has admitted that each of the individual steps is enabled in the prior art. There is not any reasonable doubt that those having ordinary skill in the art could restore immune function by regenerating a patient's involuted thymus. This is clearly established in the prior art of record. Further, Appellant has submitted evidence proving that the disclosed HGH therapy is effective for almost doubling the functional thymic mass of Appellant's own thymus. Those having ordinary skill in the art would expect that a doubling in functional thymic mass would result in an increase in thymic function. Thus, Appellant has established with reasonable certainty that the disclosed treatments are effective for restoring immune function by regenerating a patient's involuted thymus. It would be absurd to question whether those having ordinary skill in the art were capable of injecting an immunological equivalent of the tissue or organ to be transplanted into a thymus, or whether those having ordinary skill in the art were capable of transplanting an organ or grafting tissue. Appellant should not be expected to prove or demonstrate universally accepted common knowledge, i.e., that skilled surgeons exist. Thus, the evidence of record clearly shows that the claimed method can be performed based on Appellant's disclosure, and what is well known to those having ordinary skill in the art, without undue experimentation.

In support of the rejection, the Examiner has stated that "The subject matter sought to be patented as defined by the claims is not supported by an enabling disclosure." This statement is a conclusion and does not support the rejection.

The Examiner has also stated that the "instant specification only teaches the administration of arginine and DHEA and HGH and DHEA." Anyone reading the specification would understand that it teaches more than only "administration of arginine and DHEA and HGH and DHEA." The Examiner may have meant to say that the specification does not provide enablement for the claims because the only disclosed technique of

regenerating an involuted thymus is by administration of arginine or HGH, in combination with DHEA. If this is what the Examiner meant, Appellant responds by pointing out that the specification discloses additional techniques for thymic regeneration, and that a single technique for thymic regeneration would be sufficient. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. §112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Failure to disclose other techniques by which the claimed invention may be practiced does not render a claim invalid under 35 U.S.C. §112. *Spectra-physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533 3 USPQ2d 1737, 1743 (Fed. Cir.), *cert. denied*, 484 US 954 (1987). Further, as stated above, in addition to HGH therapy, Appellant has also disclosed use of zinc alone, vitamin E alone, and coenzyme Q_{10} alone for thymic regeneration and restoration of immune system function (see page 17, lines 20-26 of the specification).

The Examiner has stated that the "specification does not provide guidelines to determine thymic atrophy or involution." This is unnecessary. Appellant is not claiming a method for determining thymic atrophy or involution. Further, techniques for determining thymic atrophy or involution are well known to those having ordinary skill in the art, and need not be described, and are preferably omitted from the specification. The specification (page 3, lines 15-21) discloses that the human thymus begins to involute before the age of 20 and becomes severely atrophied by the age of 40. Thus, thymic atrophy or involution is the norm for people age 40 and over. In the absence of unusual medical conditions or the administration of substances that induce thymic regeneration, elderly patients would almost certainly have an involuted thymus, such that determination of thymic atrophy or involution is unnecessary. In the case of individuals under the age of 20, it is extremely likely that the claimed method would be unnecessary. However, all of this is well known to those having ordinary skill in the art. In the case of individuals between the ages of 20 and 40, it may be necessary or desirable to determine the extent of atrophy or involution before practicing the claimed method. This can be achieved using techniques that are well known to those having ordinary skill in the art,

e.g., magnetic resonance imaging. The specification expressly discloses that thymic regeneration may be verified by magnetic resonance imaging (page 15, lines 18-20). Magnetic resonance imaging has been well known to those having ordinary skill in the art and has been routinely used for decades.

The Examiner has stated that the "specification fails to teach that a thymus can be regenerated upon administration of human growth hormone and DHEA or human growth hormone and chromium picolinate in a patient." This is incorrect. Perhaps the Examiner meant that the specification failed to include evidence that its instructions for safely inducing thymic regeneration can be reduced to practice. However, the Examiner is well aware that these instructions do indeed result in thymic regeneration. The Appellant submitted evidence to the Examiner, and published the same evidence in the peer-reviewed scientific literature, showing that the exact instructions provided for thymic regeneration in the specification involving the administration of human growth hormone and DHEA did in fact double the functional mass of the Appellant's own thymus.

The Examiner has stated "the disclosure does not provide immunological or endocrine assays or employ experiments such as magnetic resonance imaging or morphology studies which would discern that a thymus has been regenerated." However, the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Appellant has provided in the specification specific direction and guidance for administering HGH in combination with DHEA to achieve thymic regeneration, and has submitted a declaration showing that the technique identically disclosed in the specification was successfully employed for nearly doubling the functional mass of Appellant's own thymus.

The Examiner has stated "the specification provides no guidance or working examples for intrathymic injection." Intrathymic injection is well known to those having ordinary skill in the art. A patent need not teach, and preferably omits what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ.2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v.*

Monoclonol Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied,* 480 US 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). The fact that intrathymic injection is well known to those having ordinary skill in the art is demonstrated by the fact that there are dozens of issued patents disclosing intrathymic injection, including U.S. Patent No. 4,263,279, which issued April 21, 1981, more than 23 years ago. There cannot be any serious dispute as to whether those having ordinary skill in the art would be capable of achieving intrathymic injection without undue experimentation.

The Examiner has stated "the specification fails to teach or disclose working examples for transplanting an organ or grafting of tissue." As previously stated, it is not necessary, and it is preferable that a specification does not disclose that which is well known to those having ordinary skill in the art. There is not any doubt that techniques for transplanting organs and grafting tissue are well known to surgeons possessing ordinary skill in the art, and that such surgeons routinely perform organ transplants and tissue grafts. Accordingly, the claims are enabled with respect to the step of "transplanting said organ or grafting said tissue."

The Examiner stated "the specification does not consider factors such as rejection, age-related thymic involution versus other types of thymic involution, the side effects of immunosuppressants, ALS versus CsA, the high incidence of tumors and other side effects associated with GH." A patent need not teach, and preferably omits, that which is well known in the art. Transplant surgeons routinely consider factors such as tissue and/or organ rejection. The Examiner has failed to explain why "age-related thymic involution versus other types of thymic involution" is relevant to the claimed invention. Appellant suspects that the Examiner was attempting to argue that the specification does not specifically address regeneration of a thymus that has experienced involution or atrophy due to a disease condition. Appellant is not aware of any pathological conditions that would cause an irreversibly involuted thymus, and the Examiner has failed to provide any evidence of such pathological processes that would cause irreversible thymic involution. Thus, there is not any evidence that there is an issue relating to "age-related thymic involution versus other types of thymic involution." The side

effects of immunosuppressants such as ALS and CsA are well known in the art, as admitted by the Examiner, and therefore need not be described in the specification. Further, issues relating to the side effects of immunosuppressants are not relevant to the claimed invention, which does not require or exclude the use of immunosuppressants, and does not promise a complete absence of undesirable side effects. The Examiner's reference to "a high incidence of tumors," is not relevant to the claimed invention, which does not exclude the possibility of tumors. Further, there is an absence of any evidence that growth hormone treatment causes a high incidence of hepatic tumors. The McCormick reference that the Examiner has relied on ("A Murine Model for Regeneration of the Senescent Thymus Using Growth Hormone Therapy," Kevin R. McCormick, Jack L. Haar, Jeffrey K. Taubenberger, and Richard J. Krieg, *Aging: Immunology and Infections Disease*, Volume 3, Number 1, 1991, Mary Ann Liebert Inc., Publishers) discloses at page 25 the following:

> The small size of our study population precludes a definitive finding given that the population under study is known to have a high tumor incidence. However, given the absence of tumors in placebo treated mice, these results do indicate that a correlation between growth hormone and hepatic tumors is likely.

McCormick et al. clearly stated that their experiments did not include a large enough population to make a determination as to whether growth hormone treatment causes hepatic tumors in the particular mice used in the experiments. When this admission is taken in consideration with the abundance of information showing that growth hormone therapy is effective for thymic regeneration and does not cause tumors, those having ordinary skill in the art would reasonably expect a highly desirable result, namely, an increase in functional thymic mass without a high incidence of tumors. This is especially true in view of the fact that the mice used by McCormick et al. were "known to have a high tumor incidence." Regardless, the claims are not directed to a method for transplanting organs or tissues with a guarantee that the patient will not develop tumors. Similarly, the claims are not directed to a method for transplanting organs and grafting tissue with a guarantee that there will never be any undesirable side effects associated with growth hormone therapy. Thus, each of the factors

that allegedly have not been considered in the specification are well known to those having ordinary skill in the art and/or are not relevant to enablement with respect to the claimed invention.

The Examiner has stated that "for the reasons discussed above, such experimentation would be undue for one skilled in the art at the time the invention was made." The Examiner has not provided any evidence or reasoning that would suggest that undue experimentation is needed. To the contrary, the Examiner has admitted that the individual steps are enabled. The peripheral remarks relating to side effects are not relevant to the claimed invention.

In the Final Rejection, the Examiner expanded upon previous arguments by adding that "Using the references of record, the Examiner merely stated the drawbacks, side effects and complications associated with regenerating a thymus." The fact that there may be drawbacks, side effects and/or complications associated with regenerating a thymus is not relevant to enablement. Almost all accepted therapies and surgical procedures have drawbacks, side effects and complications. The patent laws do not require that any invention must be free of all drawbacks, side effects and complications.

The Examiner has admitted that regenerating the thymus in laboratory animals is known in the art, intrathymic injection in laboratory animals is known in the art, the combination of intrathymic injection and transplantation of organs and grafting of tissue in laboratory animals is known in the art, and that transplantation of organs and grafting of tissue in laboratory animals is also known in the art. After admitting that the individual steps are known in the art, the Examiner stated as follows:

> The instant invention, however, *comprises the entire steps* [emphasis in the Final Rejection]. Applicants appear to be arguing enablement by taking apart the different steps of the invention, then using references to support the enablement for each step. The novelty of the invention is based on the entire method steps occurring in humans, not just the parts.

The Examiner has mischaracterized the invention and the point of novelty. The point of novelty relates to preparing a patient for organ or tissue transplant by stimulating deletion or anergy of the cells otherwise responsible for rejecting the transplanted tissue or organ.

Further, the method is not limited to humans, but would work equally as well in other animals. The Examiner appears to be arguing that while the individual steps are enabled, the combination is not enabled. While there may be hypothetical examples of methods that are not enabled even though the individual steps comprising the method are enabled, these examples would be limited to situations where there is an apparent conflict or impossibility. There is not any such apparent conflict or impossibility in the claims at issue. Those having ordinary skill in the art would understand that a patient's thymus may be regenerated, that a sample of material immunologically equivalent to an organ transplant may be injected into the regenerated thymus, and that an organ may be transplanted into the patient. Those having ordinary skill in the art would understand that the combination of steps is possible, and would expect, from Appellant's disclosure, that the combination would achieve the intended result, i.e., lower incidence of rejection.

The Examiner has taken the position that Dr. Fahy's Declaration is insufficient to overcome the lack of enablement rejection because it only shows an increase in functional thymic mass, not an increase in thymic function. While it is logical to expect an increase in thymic function would result from an increase in functional thymic mass, the Examiner has expressed doubts based on the Goff reference ("Growth hormone treatment stimulates thymulin production in aged dogs," *Clin. exp. Immunol.*, 1987, 68, pp. 580-587) by relying on Goff's statement that "a change (or lack of change) in thymic morphology does not prove increased or decreased thymic function; immunological or endocrine function must be assessed." However, this quote is an inappropriate overgeneralization and mischaracterization of the Goff study, and is not based on any finding of Goff et al. that thymic regeneration failed to result in increased thymic function. The opposite is in fact the case, as the rest of the disclosure teaches that there is an increase in thymic function associated with increased thymic mass. Goff's study sought: "(1) to determine concentrations of thymulin (a thymic hormone) in plasma from dogs of various ages, and (2) to evaluate the effect of bGH administration on plasma thymulin concentration and thymus morphology in middle-aged and old-aged dogs." In other words, Goff et al. used the production of thymulin by the thymus as their measurement of the

restoration of thymic function. As stated in their abstract, "Plasma thymulin concentration increased in EVERY bGH-treated dog" (emphasis added), including both dogs whose thymuses were regenerated (the middle-aged dogs) and dogs whose thymuses did not regenerate within the one-month period of study (the advanced-age dogs). Goff et al. further emphasized that "Enhancement of thymus endocrine function after bGH treatment is significant considering the immunostimulatory effects of thymulin." Thus, while there may have been some question before Goff's study as to whether an increase in functional thymic mass necessarily results in an increase in thymic function, the doubts were apparently put to rest by Goff et al., who showed that there is definitely an increase in thymic function associated with an increase in thymic mass. The Goff study showed that in the middle-aged dog population, thymic regeneration was associated with improved immunological function, as expected and as taught by the Appellant's disclosure, but that in the old-age dog population, immune function was improved even before thymic regeneration took place, implying that by the time thymic regeneration is actually observed, improved immunological function is to be expected, just as taught by the Appellant's disclosure. Therefore, rather than casting doubt on enablement, the Goff et al. reference clearly reinforces Appellant's claim that immune system function may be restored by regenerating a patient's involuted thymus.

The Examiner has next argued in the Final Rejection that "The Fahy Declaration fails to disclose the insulin levels, which are increased in the presence of HGH but dropped in the presence of DHEA." This is not relevant to the claims at issue. The claims are not directed to processes for increasing or decreasing insulin levels. Further, the specification includes working examples that show that co-administration of DHEA prevents an increase in insulin levels normally associated with HGH therapy. This is shown in experiments 1 and 2. Thus, the Examiner's statements regarding insulin level are not relevant to the claimed method, and Appellant has demonstrated that co-administration of DHEA prevents the increase in insulin levels normally associated with HGH therapy.

The Examiner repeated that "In addition, the Fahy Declaration fails to demonstrate that immune system function has been restored." As discussed above, it is respectfully submitted

that the wealth of scientific evidence very strongly suggests and demonstrates that increased thymic mass results in increased thymic function. However, as also stated above, the Goff et al. reference expressly states that increasing thymic mass causes increased thymic function, whereas the Examiner has not provided any evidence tending to show otherwise, and the Appellant knows of no valid evidence that thymic regeneration has ever been observed without an accompanying increase in thymic function. The McCormick reference described animals with tumors whose immune function was probably badly skewed as a result of tumor growth and cannot be considered representative of the normal state. Even so, McCormick did report signs that immune function was returning.

The Examiner has stated that "Both the Fahy Declaration and the specification fail to teach intrathymic injection in humans." Those skilled in the art would have known how to achieve intrathymic injection in laboratory animals, as admitted by the Examiner. There is not any reason to believe that those having ordinary skill in the art would be incapable of achieving the same in a human. It is respectfully submitted that the burden should be placed on the Examiner to show why those skilled in the art are able to achieve intrathymic injection in a laboratory animal but incapable of achieving the same in a human. Further, the claims are not limited to the treatment of humans.

The Examiner stated that "the specification fails to teach 'restoring immune system function by regenerating the patient's involuted thymus.'" The Examiner also stated that "the submitted references fail to teach intrathymic injection in humans." It is respectfully submitted that these arguments have been effectively and thoroughly rebutted above.

The Examiner next attacked Appellant's claims by arguing as follows:

> As was stated above, restoring immune system function is a limitation of the claim which the specification fails to demonstrate. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. Lack of a working example, however is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. Intrathymic injection in humans is not known in the art. As was stated above, various steps of the

> claimed method are known in the art for laboratory animals. Transplanting organs and tissue grafting of tissue are well known in the art for humans and laboratory animals. However, the instant invention is based on the entire method steps in a human. The assertion is that increased tolerance of transplants and/or grafts can occur by regenerating a thymus in addition to intrathymic injection in humans.

Except for the reference to intrathymic injection being unknown in humans, the above quoted arguments are repetitive of the Examiner's previous arguments. However, Appellant has previously addressed the fact that the claims are not limited to the treatment of humans, but are equally applicable to animal patients, and that regardless of whether intrathymic injection is known in humans or not, it does not require undue experimentation to extend intrathymic injection from animals to humans.

Appellant has effectively and completely rebutted each of the Examiner's arguments pertaining to lack of enablement. Most of the Examiner's arguments are unsupported by any evidence of record, and are contrary to the evidence of record. The Examiner's remaining arguments are not relevant to the claimed invention.

The specific reference that the Examiner has relied on for showing that there is some doubt as to whether increasing thymic mass (as shown in Dr. Fahy's Declaration) necessarily results in increased thymic function, actually demonstrates an increase in thymic function resulting from an increase in thymic mass, thus, supporting enablement for the step of "restoring immune system function by regenerating the patient's involuted thymus." The Examiner has admitted that the step of injecting the immunological equivalent of the tissue or organ to be transplanted into the patient, into the regenerated thymus" is known in the art with respect to laboratory animals. There cannot be any serious doubt that those skilled in the art would be capable of achieving the same result in humans without undue experimentation. Similarly, there cannot be any serious doubt whether surgeons skilled in the art of organ transplantation and tissue grafting would be capable of performing these activities after restoring immune function by regenerating a patient's involuted thymus and injecting the immunological equivalent of the tissue or organ to be transplanted into the regenerated thymus.

IX. Conclusion

It is apparent that the claims are enabled by Appellant's specification in view of the prior art, and that the claims are sufficiently definite to meet the requirement of 35 U.S.C. §112. For the reasons stated it is apparent that reversal of both rejections under 35 U.S.C. §112 is proper.

Respectfully submitted,

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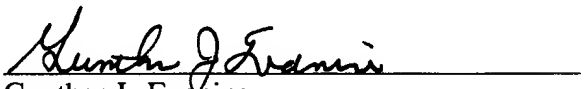
July 13, 2004
Date



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Appendix of Claims (37 CFR §1.192(c)(9))

16. A method for transplanting organs and grafting tissue into a patient comprising steps of:

restoring immune system function by regenerating the patient's involuted thymus;

injecting the immunological equivalent of the tissue or organ to be transplanted into the patient, into the regenerated thymus (or, in the case of bone marrow cells, peripherally); and

then transplanting said organ or grafting said tissue.

17. The method of claim 16 in which the step of injecting is achieved by an intrathymic injection in which said patient is given a dose of immunosuppressant at approximately the same time the intrathymic injection is administered.

18. The method of claim 17 in which the desired tissue or organ transplant is performed on the same day as the intrathymic injection, accompanied by maintenance of immunosuppression until tolerance is achieved.

19. The method of claim 17 in which transplantation of the desired organ or tissue is delayed until organ or tissue tolerance has been achieved.

20. The method of claim 16 in which said step of restoring immune system function by regenerating said patient's thymus is performed by administering a first compound consisting of one of human growth hormone, human growth hormone analogs, human growth hormone precursors, human growth hormone metabolites, human growth hormone releasers, human growth hormone mimics, and mixtures thereof in combination with a second compound consisting of one of DHEA, DHEA precursors, DHEA releasers, DHEA analogs, DHEA metabolites and combinations thereof.

21. The method of claim 16 in which said step of restoring immune system function by regenerating said patient's thymus is performed by: administering a first compound selected from the group consisting of human growth hormone, human growth hormone analogs, human growth hormone precursors, human growth hormone metabolites and human growth hormone releasers or mimics and mixtures thereof, combined with the approximately simultaneous administration of a second compound selected from the group consisting of chromium picolinate and equivalent chromium containing compounds and phenformin.

22. The method of claim 16 in which said step of restoring immune system function by regenerating said patient's thymus includes: administering zinc, Vitamin E and coenzyme Q_{10}.

32. The method of claim 16, wherein the immunological equivalent of the tissue or organs to be transplanted into the patient is endogenous material.

33. The method of claim 16, wherein the immunological equivalent of the tissue or organs to be transplanted into the patient is exogenous material.

34. The method of claim 22 in which said zinc is administered at 30-130 mg/60 kg body weight per day; Vitamin E is administered at 200-1000 IU/day/60 kg of body weight; and coenzyme Q_{10} is administered at 10-200 mg/day.